From the INTERNATIONAL SEARCHING AUTHORITY

VOSSIUS & PARTNER Siebertstrasse 4 D=81675 Münchenger

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

| GERMANY | E.AGEGANGEN Vossius & Partner 28. April 2004 | (PCT Rule 44.1) |
|------------------------------------|--|---|
| | Frist mm | Date of mailing (day/month/year) 26/04/2004 |
| Applicant's or age G 2536 PCT | nt's file reference | FOR FURTHER ACTION See paragraphs 1 and 4 below |
| International applic | | International filing date (day/month/year) 12/11/2003 |
| Applicant MICROMET AC | 3 | |
| Filing of The appli | amendments and statement under Article 19: icant is entitled, if he so wishes, to amend the claim | · · · · · · · · · · · · · · · · · · · |
| When? | The time limit for filing such amendments is normal International Search Report; however, for more de | |
| Where? | Directly to the International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41–22) 740.14.35 | 5 |
| For more | e detailed instructions, see the notes on the acco | mpanying sheet. |
| | icant is hereby notified that no International Search (2)(a) to that effect is transmitted herewith. | n Report will be established and that the declaration under |
| 3. With reg | ard to the protest against payment of (an) addition | onal fee(s) under Rule 40.2, the applicant is notified that: |
| | | n transmitted to the International Bureau together with the test and the decision thereon to the designated Offices. |
| no c | decision has been made yet on the protest; the app | olicant will be notified as soon as a decision is made. |
| 4. Further action | n(s): The applicant is reminded of the following: | |
| If the application priority claim, | nt wishes to avoid or postpone publication, a notice | oplication will be published by the International Bureau. e of withdrawal of the international application, or of the in Rules 90 <i>bis</i> .1 and 90 <i>bis</i> .3, respectively, before the ation. |
| | | al preliminary examination must be filed if the applicant onths from the priority date (in some Offices even later). |
| Within 20 mon | ths from the priority date, the applicant must perfor | rm the prescribed acts for entry into the national phase |

| Name and mailing address of the International Searching Authority | Authorized officer |
|---|--------------------|
| European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Anu Evers |

before all designated Offices which have not been elected in the demand or in a later election within 19 months from the

priority date or could not be elected because they are not bound by Chapter II.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

Notes to Form PCT/ISA/220 (first sheet) (January 1994)

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 *Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
 claims 30, 33 and 36 unchanged; new claims 49 to 51 added.*
- [Where originally there were 15 claims and after amendment of all claims there are 11]: "Claims 1 to 15 replaced by amended claims 1 to 11."
- [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
 "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
 "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- 4. [Where various kinds of amendments are made]: "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.



PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference | (Form PCT/ISA/2 | of Transmittal of International Search Report 20) as well as, where applicable, item 5 below. |
|--|---|--|
| G 2536 PCT | ACTION | <u> </u> |
| International application No. | International filing date (day/month/year) | (Earliest) Priority Date (day/month/year) |
| PCT/EP 03/12664 | 12/11/2003 | 13/11/2002 |
| Applicant | | |
| MICROMET AG | | |
| This International Search Report has been according to Article 18. A copy is being tra | n prepared by this International Searching Authansmitted to the International Bureau. | nority and is transmitted to the applicant |
| This International Search Report consists It is also accompanied by | of a total of7 sheets. a copy of each prior art document cited in this | report. |
| Basis of the report | | |
| | international search was carried out on the bas ess otherwise indicated under this item. | sis of the international application in the |
| the international search w Authority (Rule 23.1(b)). | as carried out on the basis of a translation of the | ne international application furnished to this |
| b. With regard to any nucleotide an was carried out on the basis of the | e sequence listing: | ternational application, the international search |
| | nal application in written form. | 2 |
| | rnational application in computer readable form | |
| | this Authority in written form. | |
| | this Authority in computer readble form. sequently furnished written sequence listing d | oes not go beyond the disclosure in the |
| | s filed has been furnished. | identical to the written engagement liction has been |
| furnished | лтавоп тесогаеа вт сотрыет теасаые тогт в | s identical to the written sequence listing has been |
| 2. Certain claims were fou | nd unsearchable (See Box I). | |
| 3. X Unity of invention is lack | king (see Box II). | |
| 4. With regard to the title, | | |
| X the text is approved as su | bmitted by the applicant. | |
| the text has been establis | hed by this Authority to read as follows: | |
| 5. With regard to the abstract, | | |
| X the text is approved as su | bmitted by the applicant. hed, according to Rule 38.2(b), by this Authoril | ty as it appears in Box III. The applicant may |
| | date of mailing of this international search rep | |
| 6. The figure of the drawings to be publ | ished with the abstract is Figure No. | 1 |
| as suggested by the appli | cant. | None of the figures. |
| X because the applicant faile | ed to suggest a figure. | |
| because this figure better | characterizes the invention. | |

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/542 G01N33/566

C. DOCUMENTS CONSIDERED TO BE RELEVANT

G01N33/569

CO7K16/28

G01N15/14

Relevant to claim No.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\label{eq:minimum documentation searched (classification system followed by classification symbols)} IPC~7~~GO1N~~CO7K$

Category ° Citation of document, with indication, where appropriate, of the relevant passages

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE, CHEM ABS Data

| Y TOWNSEND S E ET AL: "Single emultiple staining to detect unifrequency B cells" JOURNAL OF IMMUNOLOGICAL METHORSCIENCE PUBLISHERS B.V., AMSTER vol. 249, no. 1-2, 1 March 2001 (2001-03-01), page XP004317478 ISSN: 0022-1759 page 139; figure 2 | ODS, ELSEVIER RDAM, NL, |
|--|---|
| X Further documents are listed in the continuation of box C. | -/ χ Patent family members are listed in annex. |
| *Special categories of cited documents: *A* document defining the general state of the art which is not considered to be of particular relevance *E* earlier document but published on or after the international filing date *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed | 'T' later document published after the international filing date or priorily date and not in conflict with the application but cited to understand the principle or theory underlying the invention 'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone 'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. '&' document member of the same patent family |
| Date of the actual completion of the international search 16 April 2004 | Date of mailing of the international search report $26/04/2004$ |
| Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | Authorized officer Diez Schlereth, D |

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International Application No PCT/EP 03/12664

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| | | |
| Υ | KUBITSCHECK U ET AL: "FLUORESCENCE RESONANCE ENERGY TRANSFER ON SINGLE LIVING CELLS APPLICATION TO BINDING OF MONOVALENT HAPTENS TO CELL-BOUND IMMUNOGLOBULLN E" BIOPHYSICAL JOURNAL, NEW YORK, US, US, vol. 60, August 1991 (1991-08), pages 307-318, XP000882076 ISSN: 0006-3495 page 311 | 1-25 |
| Α | KOKSCH M ET AL: "Fluorescence resonance energy transfer as a new method for the epitope-specific characterization of anti-platelet antibodies" JOURNAL OF IMMUNOLOGICAL METHODS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 187, no. 1, 16 November 1995 (1995-11-16), pages 53-67, XP004020967 ISSN: 0022-1759 page 57-60 | 1-25 |
| А | LUNDIN K ET AL: "Development of a time-resolved fluorescence resonance energy transfer assay (Cell TR-FRET) for protein detection on intact cells" ANALYTICAL BIOCHEMISTRY, ORLANDO, FL, US, vol. 299, no. 1, 1 December 2001 (2001-12-01), pages 92-97, XP002269887 ISSN: 0003-2697 figure 1 | 1-25 |
| Α | US 5 213 960 A (CHANG TSE W) 25 May 1993 (1993-05-25) column 7, line 45 -column 8, line 25 | 1-25 |
| X | US 2002/006403 A1 (YU XUE-ZHONG ET AL) 17 January 2002 (2002-01-17) page 1, paragraph 12 | 26 |
| X | WO 00/26667 A (MILLER JONATHAN L) 11 May 2000 (2000-05-11) figure 2; examples SEQ,44 | 27 |
| х | DE 100 19 967 A (FENNING BIOMED GMBH DR) 25 October 2001 (2001-10-25) examples SEQ,7-8 | 27 |
| X | WO 01/98361 A (GENENTECH INC ;DEVAUX BRIGITTE (US); HONGO JO ANNE S (US); SHELTON) 27 December 2001 (2001-12-27) examples SEQ,8 | 27 |
| | -/ | |

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International Application No PCT/EP 03/12664

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| | passages | To Start to Oldin No. |
| | WO 01/29538 A (BECTON DICKINSON CO) 26 April 2001 (2001-04-26) page 8-10; figure 2 | 28 |
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-28

method and tools for identifying antigen-specific B cells

- 1.1. Claims: 1-25
 method for identifying a B cell carrying a surface
 immunoglobulin
- 1.2. Claim: 26 antibody specific for human CD28
- 1.3. Claim: 27
 antibody comprising an amino sequence selected from
 the group consisting of SEQ ID No 76,78,80,82,84,86
 and 88 and/or which is encoded by a nucleic acid
 sequence comprising a sequence selected from the group
 SEQ ID No 77,79,81,83,85,87,89,60 and 61.

It is noted that this subinvention can be also splitted in different sub-subinventions because some of the above sequences are already known from the state of the art.

1.4. Claim : 28 flow cytometer device

It is not apparent at the present stage what can be taken as common novel and inventive concept within the sense of Rule 13 PCT for linking the subject-matter of independent claims 1, 26, 27 and 28.

Please note that all inventions mentioned under item 1; although not necessarily linked by a common inventive concept, could be searched without effort justifying an additional fee.

International application No. PCT/EP 03/12664



| Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet) |
|---|
| This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: |
| 2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet) |
| This International Searching Authority found multiple inventions in this international application, as follows: |
| see additional sheet |
| As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. |
| 2. X As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| 4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: |
| Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees. |

Information on patent family members



PCT/EP 03/12664

| Patent docur cited in search | | Publication date | | Patent family member(s) | | Publication date |
|---------------------------------|----------|------------------|--|--|-------------------------|--|
| US 521396 | 50 A | 25-05-1993 | AU US WO US | 3785493 5326696 9318068 5256542 | A A1 | 05-10-1993 05-07-1994 16-09-1993 26-10-1993 |
| US 200200 | 06403 A1 | 17-01-2002 | NONE | | | |
| WO 002666 | 57 A | 11-05-2000 | AU CA EP JP WO | 1458500 2317808 1051620 2002529054 0026667 | A1 A1 T | 22-05-2000 11-05-2000 15-11-2000 10-09-2002 11-05-2000 |
| DE 100199 | 967 A | 25-10-2001 | DE AU WO | 10019967 7395001 0181423 | Α | 25-10-2001 07-11-2001 01-11-2001 |
| WO 019836 | 51 A | 27-12-2001 | AU BR CA CN EP JP WO | 7142201 0112272 2412494 1447857 1292680 2004500873 0198361 | A A1 T A2 T | 02-01-2002 06-05-2003 27-12-2001 08-10-2003 19-03-2003 15-01-2004 27-12-2001 |
| WO 012953 | 38 A | 26-04-2001 | EP JP WO | 1222451 2003512616 0129538 | T | 17-07-2002 02-04-2003 26-04-2001 |